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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/158,272	09/22/1998	VINCENTE DIAS	10806-64	3752

7590 06/17/2003

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EXAMINER	
WOITACH, JOSEPH T	
ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 06/17/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

File

Office Action Summary

Application No.	Applicant(s)
09/158,272	Dias et al.
Examiner	**Art Unit**
Joseph Woitach	1632

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Apr 7, 2003*.

2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *27, 28, 33, 35-44, 46, 47, 50, 53, 55-57, and 60-67* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☒ Claim(s) *28, 43, 44, 46, 47, 55-57, 64, and 65* is/are allowed.

6) ☐ Claim(s) _____ is/are rejected.

7) ☒ Claim(s) *27, 33, 35-42, 50, 53, 60-63, 66, and 67* is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☒ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☒ All b) ☐ Some* c) ☐ None of:

1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

This application filed September 22, 1998, claims benefit of provisional application 60/062,994, filed October 23, 1997, and claims priority to foreign application 9703663-6 filed October 8, 1997 in Sweden.

Applicants' amendment filed April 7, 2003, paper number 27, has been received and entered. Claims 32, 45, 48, 49, 54 and 59 have been canceled. Claims 27, 28, 33, 35-43, 50, 53, 55-57, 60-61, 64 and 65 have been amended. Claims 66 and 67 have been added. Claims 27, 28, 33, 35-44, 46, 47, 50, 53, 55-57 and 60-67 are pending and currently under examination.

Claim Objections

Claims previously objected to because they are not specifically drawn to the elected invention of methods of genetic modification in transgenic animals is withdrawn.

In light the claim amendments and in view of Applicants' arguments, Examiner agrees that the instantly claimed invention no longer encompasses Group IV, methods of use *in vivo* or other non-elected inventions.

Newly amended claims 39 and 40 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper

dependent form, or rewrite the claim(s) in independent form. In the instant case, 'direct repeats' (claim 39) and 'indirect repeats' (claim 40) is broader than 'six sites' indicated in claim 27.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 27, 28, 33, 35-44, 46, 47, 50, 53-57 and 60-65 rejected under 35 U.S.C. 112, first paragraph, is withdrawn.

The amendments to the independent claims to encompass the practice of the method *in vitro*, and amending the claims to encompass the specific embodiments previously set forth in the basis of the rejection has obviated the basis of the rejection.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 27, 28, 33, 35-44, 46, 47, 50, 53, 55-57 and 60-65 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn.

Amendments to the claims have obviated the specific basis of each of the rejections.

Double Patenting

A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

Claims 37 and 39 are objected to under 37 CFR 1.75 as being a substantial duplicate of claim 35. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Claims 38 and 40 are objected to under 37 CFR 1.75 as being a substantial duplicate of claim 36. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing

one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Claim 60 is objected to under 37 CFR 1.75 as being a substantial duplicate of claim 27. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Claim 61 is objected to under 37 CFR 1.75 as being a substantial duplicate of claim 53. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Claim 66 is objected to under 37 CFR 1.75 as being a substantial duplicate of claim 67. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

In each case the objected claims encompass exactly the same embodiments for each of the claimed inventions. All the methods have been amended to be practiced *in vitro* and any intended use recited in the preamble of the method claims does not further limit the claim because the same method steps are practiced in each case. It may be that providing more method

steps to distinguish methods and more specifically set forth methods directed to the intended use may distinguish the method claims one from another. With respect to the dependent claims reciting that the cell factor HMG1 chromatin-associated protein is present does not further limit the claim because this factor is supplied by the cell and required for the method to work. No other mammalian factor other than HMG1 chromosome-associated protein is disclosed to function in the claimed method

Conclusion

Claims 28, 43, 44, 46, 47, 55, 56, 57, 64, 65 are allowed. Claims 33, 41, 42, 62, 63 are objected to for being dependent on rejected claims. Claims 27, 35-40, 50, 53, 60, 61, 66 and 67 are objected to for being duplicate claims.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however,

will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Claims 27, 28, 32, 33, 35-50, 53-57 and 59-65 are free of the are of record because the art fails to teach or make obvious the use of beta recombinase in transgenic animal methodology. At the time of filing a prokaryotic Beta recombinase was isolated from a Gram-positive broad host range plasmid PSM19035, originally isolated from *S. pyogenes* and shown to require additionally host cofactors, such as Hbsu from *S. subtilis,* to affect recombination between two *six* site target sequences. Though at the time of filing beta recombinase was known in the art as a member of the resolvase/invertase family of recombinases, and other recombinases (Cre and Flp) were used in the art in the generation of transgenic animals, these recombinases are classified in the Int family of recombinases. Importantly, the Int family of recombinases do not require additional cofactors. The present specification is the first to demonstrate that other host non-prokaryotic factors, such as the mammalian cofactor HMG, are able to serve as host factors in the presence of beta recombinase and polynucleotide sequences between two *six* sites in generating an intramolecular recombination event in mammalian cells.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph Woitach whose telephone number is (703)305-3732.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Reynolds, can be reached at (703)305-4051.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group analyst Dianiece Jacobs whose telephone number is (703) 308-2141.

Papers related to this application may be submitted by facsimile transmission. Papers should be faxed via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center numbers are (703)308-4242 and (703)305-3014.

Joseph T. Woitach

Deborah Crouch

DEBORAH CROUCH
PRIMARY EXAMINER
GROUP ~~1800~~ 1630